

REMARKS

Claims 9-23 are pending. Claims 1-8 were cancelled. Claims 9, 11 and 16 were amended. No new matter was introduced by these amendments. Accordingly the amendments are fully supported and no additional search on the part of the Office. Moreover, the amendments provided above place the pending claims in condition for allowance. The amendments also frame the issues which will be address on appeal, if necessary. Support for the assertions made below is provided relative to the substitute specification submitted on October 4, 2004. Thus, entry of the amendments and reconsideration of the claims in view of the amendments and the remarks below is respectfully requested.

Supported by a Specific, Substantial and Credible Utility

Claims 9-23 were rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific, substantial or credible asserted utility or a well established utility. The present rejection does not treat each of these utility requirements separately but instead improperly lumps them together when alleging a lack of utility. In response, Applicants traverse this rejection and demonstrate that the pending claims are adequately supported by a specific, substantial and credible utility.

To satisfy the utility requirement an applicant for a patent must assert a specific, substantial and credible utility. *Cross v. Iizuka*, 753 F.2d 1040, 1044 (Fed. Cir. 1985). Applicants have asserted a number of uses for the claimed subject matter which satisfy the exceedingly low burden raised by the law and the Constitution. Once a utility has been asserted, it is the Office's initial burden to establish whether it is more likely than not that a skilled artisan would consider an asserted utility to be specific, substantial and credible. *In re Brana*, 51 F.3d 1560, 1566, (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such person of the invention's asserted utility."); and MPEP § 2107 II(B)(1)(ii).

The Invention is Useful to Treat Multiple Sclerosis

The text of the specification asserts a number of uses for the claimed invention. For example, the specification asserts that particular embodiments of the disclosed invention are useful for the treatment of tissue specific autoimmunity, degenerative autoimmunity, rheumatoid arthritis, atherosclerosis, multiple sclerosis, vasculitides, delayed hypersensitivities, skin grafting, a transplant, spinal injury, stroke, neurodegeneration, and ischemia. **Specification at [0169]**. For the purposes of this discussion, the claimed antibodies are useful to treat multiple sclerosis. This asserted utility is a specific, substantial, and credible, and therefore fulfills the requirement under 35 U.S.C. § 101.

The Office has alleged that Applicants have not identified a “specific pathway in a specific cell type that leads to a specific disease.” Office Action, page 3. Applicants disagree. The present specification identifies multiple sclerosis as a disease state that can be treated by modulating OX2R activity. The specification also notes that cells of the myeloid lineage, which include mast cells, can be down regulated as a therapeutic treatment.

“In cases where leukocytes, including macrophage/**myeloid lineage cells**, expressing the OX2R are involved in pathologies and contribute to the disease process, **it may be desirable to inhibit the function of these cells**. This may be achieved by appropriate stimulation of an OX2R, such that the cell-inhibitory activities of receptor signalling [sic] are mobilized. **This may be achieved using, e.g., a ligand OX2 agonist or an antibody to the OX2R that has agonistic activities for the receptor.**” *Id.* (emphasis added.)

As such, the specification as filed identifies particular diseases, a specific pathway and specific cell types which are responsible for the disease. Thus, this particular utility presently asserted by Applicants is explicitly disclosed in the specification.

The Office also allegation in the last Office Action that art cited in support of the asserted utility was “post filing art” and therefore could not be used to support Applicants’ position. This is incorrect as a matter of law.

Specific Utility

The specific utility aspect of the utility requirement mandates that an applicant for a patent assert a specific, rather than a general or nebulous use for the claimed subject matter. In a recent

pronouncement on the subject, the Federal Circuit wrote that “a specific utility is particular to the subject matter claimed and would not be applicable to a broad class of invention.” *In re Fisher*, 421 F.3d 1365, 1372 (*citing* MPEP §2107.01)(Fed. Cir, 2005). The court pointed to nebulous expressions of utility like “biological activity”, “biological properties” or “useful for technical and pharmaceutical purposes” as examples of asserted utilities which were not sufficiently specific. *Id.* at 1371. In contrast to these general, nebulous assertions of utility, Applicants assert that the claimed antibodies or binding fragments thereof which bind to SEQ ID NO:20 are useful to treat multiple sclerosis. The asserted utility does not apply to any random antibody but instead is specific to antibodies that bind to the recited protein. There is nothing non-specific about this asserted utility. Applicants submit that this assertion of utility is sufficiently specific to satisfy the statutory requirements imposed by 35 U.S.C. § 101. The Office Action does not provide any reasons whatsoever to support the allegation that the asserted utility is non-specific. Accordingly, Applicants’ position is that there is no issue as to whether the pending claims are supported by a specific utility.

Substantial Utility

The substantial utility aspect of the utility requirement asks an applicant to assert a utility that defines a “real world” or a “practical” use. MPEP § 2107.01. “‘Practical utility’ is a shorthand way of attributing ‘real-world’ value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.” *Nelson v. Bowler*, 626 F.2d 853, 856 (C.C.P.A. 1980) Any reasonable use asserted by an applicant that provides a public benefit “should be accepted as sufficient, at least with regard to defining a ‘substantial’ utility.” *Nelson* at 856; *see also* MPEP §2107.01.

Applicants have asserted that the claimed subject matter is useful to treat multiple sclerosis. The Office has not alleged that this asserted utility is insubstantial. Accordingly, Applicants submit that there is no issue as to whether the pending claims are supported by a substantial utility.

Credible Utility

The final aspect of the utility requirement relates to the credibility of the asserted utility. “To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful

result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992) (emphasis added). As discussed in the M.P.E.P. at section 2107.01, situations where an invention is completely inoperative are rare and examples where the rejection has been upheld on appeal are rarer still. The Office has alleged that the asserted utility is not credible. Applicants submit that one of ordinary skill in the art would conclude after reviewing the specification and in light of the general knowledge available in the relevant art at the time the application was filed, that the asserted utility was credible.

The Office alleged that the asserted utility would not be credible to one of ordinary skill in the relevant art because the specification allegedly did not teach any specific diseases which resulted from activity of the OX2 receptor (OX2R). Office Action, page 3. The Office also alleged that the specification failed to teach a link between the function of the OX2R receptor and multiple sclerosis. *Id.* at 4. Applicants disagree. The following discussion provides specific examples of support provided in the specification as well as references in the art which show that Applicants' asserted utility regarding modulation of the OX2-OX2R interaction to treat multiple sclerosis (MS) was credible. The references cited below in support of this argument are supplied with the present response and submitted for consideration by the Office.

Contrary to the allegations raised by the Office, the assertion that the claimed subject matter is useful to treat MS is credible because those of ordinary skill in the art recognized a link between the OX2R and MS. Those of ordinary skill in the art would have recognized, after reviewing the present specification, that the claimed subject matter was useful for treating MS because: 1) cells of the myeloid lineage (such as mast cells) were thought to play a role in the development of MS; 2) OX2R was known to be expressed on cells of the myeloid lineage, including mast cells; 3) OX2R was known to play a role in signal transduction, and 4) altering the interaction of OX2 with the OX2 receptor impacts mast cell activity. This information when taken as a whole, provides sufficient support for one of ordinary skill in the art to consider the asserted utility to be credible.

The role that mast cells play in the onset and severity of MS has been shown in the experimental autoimmune encephalomyelitis model (EAE). The murine EAE model is recognized in the relevant art as the "prototypical rodent model of human multiple sclerosis." **Secor, et al.**,

(March 2000) *J. Exp. Med.* 191:813-821. The EAE model was also recognized as a model for human MS well before the filing date of the present application. *See Steinman, L. (1996) Cell* 85:299-302; French-Constant, C. (1994) *Lancet* 343:271-275; and Kermode, A.G. (1990) *Brain* 113:1477-1489.

It has been reported that that mast cell activity played a role in EAE prior to the filing of the present application. Lafaille, *et al.* (1994) *J. Exp. Med.* 186:307-312, 311. Lafaille, *et al.* did not teach or suggest a role for OX2R. This causative role for mast cells in EAE was supported in part by observation that mast cell protease levels were elevated in the cerebrospinal fluid of MS patients. Rozniecki, *et al.*, (1995) *Ann Neurol.* 37(1):63-66. It was also known that mast cell proteases were capable of degrading myelin. Dietsch & Hinrichs, (1991) *Cell Immunol.* 135(2):541-548. This observation further supports a role for mast cells in EAE.

The specification discloses that the OX2R receptor is expressed on cells of the myeloid lineage, including monocytes, granulocytes, and mast cells. **Specification at [0169] and [0170].** Regarding the function of the receptor, features of the OX2R amino acid sequence suggest that the receptor is involved in signal transduction. **Specification at [0003].** The specification further notes that the OX2RH1 class of OX2R homologs (which includes SEQ ID NO:20) has motifs suggestive of receptor signaling via a tyrosine kinase pathway. **Specification at [0085].** In addition to the specification, the art had accepted the role that the OX2R played in signal transduction prior to the filing date of the present application. Preston, *et al.* (1997) *Eur. J. Immunol.* 27:1911-1918 (of record). Thus, the teachings of the specification taken with work in the art clearly suggest that the OX2R plays a role in signal transduction.

The specification teaches that the EAE system can be used to study the role of OX2R. **Specification at [0170].** The specification's disclosure regarding OX2R and EAE is supported by published observations showing that blocking the interaction of OX2R with the OX2 ligand using an OX2R monoclonal antibody exacerbated symptoms observed in an experimental allergic encephalomyelitis model. Wright, *et al.* (Aug. 2000) *Immunity* 13(2):233-242, 233 (abstract). Thus, the teachings of the specification, as confirmed with the post-filing data of Wright, *et al.* support the assertion that the OX2R plays a role in MS.

Applicants submit that the discussion provided above is more than adequate to demonstrate that the asserted utility for the claimed invention was adequately supported by the application when it was filed. Accordingly, the present rejection alleging a lack of utility for the claimed subject matter should be withdrawn.

The Pending Claims are Supported by an Adequate Written Description

Claims 9-14 and 16-23 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Specifically, the Office alleged that “open” claim language describing an antibody or fragment thereof that bound to an amino acid sequence consisting essentially of SEQ ID NO:20 did not enjoy adequate support in the specification. Applicants disagree with this interpretation of the claimed subject matter. Applicants intended to claim an antibody that bound to an antigen formed by a portion of the amino acid sequence of SEQ ID NO:20. Nevertheless, solely to place the present claims in condition for allowance or appeal, Applicants have amended claim 9 to clarify the relationship of the binding specificity of the claimed antibody to the amino acid sequence of SEQ ID NO:20. This amendment overcomes the present rejection.

The Pending Claims are Supported by an Enabling Disclosure

Claims 9-23 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. In addition to the lack of enablement resulting from the alleged lack of utility discussed above, the Office also alleged that “open” claim language describing an antibody or fragment thereof that bound to SEQ ID NO:20 did not enable a skilled artisan to make and use antibodies to all possible fusion partners of SEQ ID NO:20.

In view of the remarks above, Applicants submit that the claimed subject matter is useful and therefore the portion of the present enablement rejection based on the 35 U.S.C. § 101 rejection has been overcome. Moreover, Applicants submit that the additional reasons offered by the Office in favor of the present enablement rejection are overcome by the amendments to claims which specify that the claimed antibodies bind to an antigen of SEQ ID NO:20. As such, the enablement rejection of the pending claims should be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 140942000900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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